

Clustering and Micro-immiscibility in Alcohol-Water Mixtures: Evidence from Molecular Dynamics Simulations

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We have investigated the hydrogen-bonded structures in liquid methanol and a 7:3 mole fraction aqueous solution using classical Molecular Dynamics simulations at 298K and ambient pressure. We find that, in contrast to recent predictions from X-ray emission studies, the hydrogen-bonded structure in liquid methanol is dominated by chain and small ring structures. In the methanol-rich solution, we find evidence of micro-immiscibility, supporting recent conclusions derived from neutron diffraction data.

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INTRODUCTION

The molecular structure and dynamics of hydrogen-bonded networks is of fundamental importance across a wide range of scientific disciplines. The tetrahedral hydrogen-bonded structure of water is well-known and continues to be extensively studied. Methanol, as the simplest alcohol, differs only in the presence of a methyl group in place of a proton, but is known to adopt a very different structure to water, comprising hydrogen-bonded chains and ring structures. The structure and topology of the hydrogen-bonded network in pure methanol and its aqueous solutions is an area where open questions still remain as to the dominant structural motifs. Conclusions drawn from recent experimental studies are conflicting [1, 2, 3]. This paper presents results of classical Molecular Dynamics (MD) simulations that characterise the hydrogen-bonded clusters and the micro-immiscibility of the aqueous solution.

Computer simulations have become increasingly used to aid predictions of structure and liquid methanol is a good example of a widely-studied system. Investigations have ranged from simple pair potential calculations (e.g. [4] and refs. therein), through to the use of Monte Carlo methods to fit and interpret experimental data [2], and now, to full *ab initio* studies of the structure and properties of the liquid [5, 6]. In addition, hybrid schemes combining the rigour of first principles approaches and the expediency of pair potentials have also been applied [7].

Methanol is also the simplest amphiphilic molecule and its aqueous solutions are prototypical systems to study hydration of the hydrophobic and hydrophilic moieties. It is structurally as simple as an amphiphile can be, yet its aqueous solutions exhibit the characteristic thermodynamic non-ideality of more complex systems. The traditional molecular-level description of hydration of hydrophobic species is enhancement of the structure of water immediately surrounding the hydrophobic group, leading to ice-like or clathrate structures [8]. Within this model, association of hydrophobic species is entropy-

driven, liberating structured water. For decades, this has been believed to explain the smaller than expected entropy change upon mixing (based on what might be expected for ideally mixed solutions). In recent years, this view has begun to be challenged by predictions from both computational [9] and experimental [3] studies investigating the structure and properties of alcohol-water mixtures.

Investigations of methanol-water mixtures have provided compelling counter-evidence to the traditional view of enhanced water structure around hydrophobic groups. MD simulations by Meng and Kollman [10], Laaksonen *et al* [9] and Fidler and Roger [11] point to preservation rather than enhancement of the water structure around the methyl group. Experimentally, Dixit *et al* [3] have employed the Empirical Potential Structure Refinement (EPSR) method to analyse data from neutron diffraction (ND) experiments and suggest the anomalous thermodynamics is due to incomplete mixing of water and methanol. This result is the most direct challenge to the ‘iceberg’ model and suggests that rather than being enhanced or depleted, the structure of water in the mixture is surprisingly close to that of the pure liquid. Further evidence of incomplete mixing has been presented very recently by Guo *et al* [1], on the basis of X-ray emission (XE) spectroscopy. There are, however, apparent inconsistencies between these experimental studies; the small fraction (~ 0.13) of the water molecules predicted to exist singly (i.e. ‘singletons’, with no hydrogen-bonds to other water molecules) by Dixit *et al* is suggested to be incompatible with the simulated XE spectra of Guo *et al*.

The aims of this paper are twofold. Utilising classical MD simulations, we investigate the cluster structures and their lifetimes in methanol, in order to provide insight into conflicting predictions from recent experimental studies as to the dominant structural motifs in the pure liquid. We also present results from simulations of a 7:3 mole fraction aqueous solution, specifically aimed at providing molecular level insight into the predicted micro-immiscibility of aqueous methanol. On the basis

of our analysis, we are able to predict the predominant hydrogen-bonded structures in pure methanol and the changes these undergo upon hydration. In addition we show that a 7:3 aqueous solution does exhibit immiscibility on a microscopic scale, and we characterise the structure and lifetimes of water clusters within the solution.

CALCULATION DETAILS

We have performed classical MD simulations within the *NVT* and *NPT* ensembles at 298K and ambient pressure. The classical simulations utilised previously tested potential parameters for both water [12] and methanol [13, 14] that have been demonstrated to give good predictions of the single component liquid structure and dynamics, at both ambient and elevated pressures, in comparison to experimental data. Both molecules are modelled as fully flexible entities, with van der Waals non-bonding interaction terms for each type of atom. Within the DLPOLY [15] program suite, we have performed *NVT* simulations over 2ns duration with a timestep of 0.5fs on system sizes as follows: pure methanol, 512 molecules in a cubic box of size 33.03Å; 7:3 mixture, 297 methanol molecules and 127 waters, in a cubic box of edge 28.5Å, corresponding to a density of the 7:3 mixture of 846 kg m^{-3} , in close agreement with the experimentally measured density of 842 kg m^{-3} [3]. Trajectory snapshots were saved every 0.1ps for analysis. All simulations were equilibrated for 0.5ns prior to data collection. Post-simulation analysis of the trajectories allowed calculation of the self diffusion coefficients (via the Einstein relationship [16]) and site-site radial distribution functions (RDFs), $g(r)$.

The trajectory data was also used to characterise cluster distributions. The clustering algorithm was similar to that described previously to analyse data from the EPSR procedure [3], originating from the formalism of Geiger *et al* [17]. A molecule is defined to be a member of a cluster if its oxygen atom is found to be within R_{cut} of a neighbouring oxygen atom in the cluster (where R_{cut} is the first minimum in the oxygen-oxygen RDF, which is ~ 3.5 Å for both methanol and water species). Defining a cluster in such a manner includes no angular prescriptions, and Pagliai *et al* [5] have suggested tighter geometrical requirements, to eliminate unphysical clustering arrangements, including a HO–O angle smaller than 30 degrees. Analysis of a representative fraction of clusters predicted by our algorithm indicates that the overwhelming majority of clusters satisfy these additional constraints.

An open question regarding the hydrogen-bonded structure in liquid methanol is the suggested predominance of cyclic clusters [1]. We have calculated the proportion and distribution of sizes of cyclic clusters using an algorithm that iteratively ‘prunes’ the clusters previously identified to remove branches and non-cyclic struc-

tures. This procedure removes all linear and branched structures, leaving only cyclic structures which are either pure ‘n-mers’ (single rings) or compound cycles comprising smaller cyclic structures.

Cluster lifetimes were also deduced from the trajectory data, by calculating the average duration that a molecule remains a participant in a cluster. A cluster is deemed to have ‘survived’ between successive trajectory snapshots if at least one member molecule remains the same. The distinction is made between the lifetimes of singletons (a cluster size of 1) and other cluster sizes.

RESULTS

Details of the structural predictions from the simulations of pure water and methanol have been reported elsewhere [12, 13]. Here we note only that in both cases, the bulk transport properties and the radial distribution functions (RDFs) are in good agreement with experimental data. However, in the case of pure methanol, we do present an analysis of the hydrogen-bonded network in the light of recent claims by Guo *et al* [1], who claim 6-ring and 8-chain motifs to be the predominant structural feature in liquid methanol, in accordance with previous work [18] that had fitted the geometry of hexameric methanol units to X-ray diffraction data. Guo *et al* additionally claim that ring and chain structures are present in equal abundance. This is in contrast to the predictions made by Pálinkás *et al* [2] on the basis of reverse Monte Carlo fitting of ND data, employing a rigid, united atom structural model to describe methanol. This Monte Carlo study found no such predomination of hexameric rings; the average cycle size was predicted to be 4 molecules. In addition, it was found that cyclic structures comprise only about one third of the total clusters of methanol, that the average length of hydrogen-bonded chains is also approximately 4 molecules and 15% of the methanol molecules exist as singletons.

The results of analysis of our MD simulations for clusters in pure methanol is shown in Figure 1. The number of clusters containing i molecules is plotted as a fraction of total number of clusters, $m(i)/M$ (where $M = \sum_i m(i)$) against the cluster size i . Of these clusters, we identify those containing cyclic structures, and plot the distribution of such clusters, $m_r(j)/M_r$, as a function of ring size, j . We find that nearly 99% of the methanol molecules exist in clusters of two molecules or more, but as a fraction of the total number of clusters, the singleton species account for a little over a quarter of all clusters found. The average cluster size is 23 molecules, but this is rather skewed by the presence of a small number of very large clusters. The figure shows that the proportion of clusters decreases rapidly with increasing cluster size. Analysis of cyclic structures present within clusters indicates that the most common cyclic structures

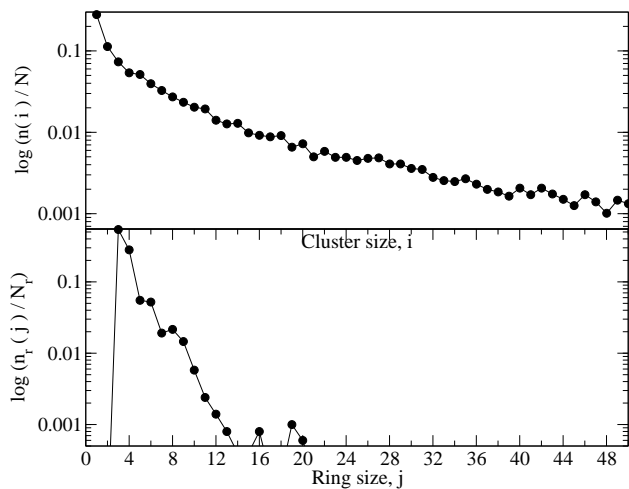


FIG. 1: Clustering in pure methanol. The figure shows the fraction of molecular clusters (upper panel) and rings (lower panel)

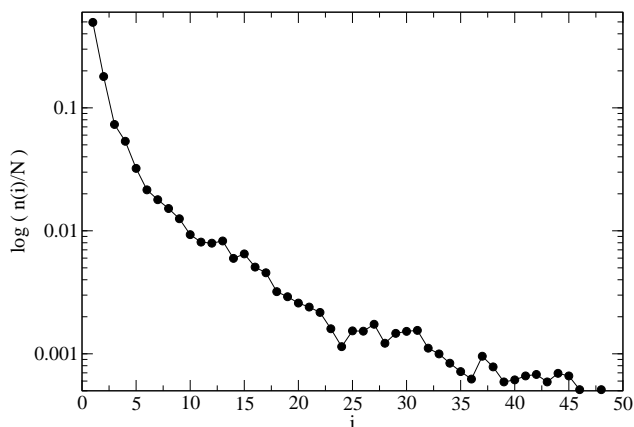


FIG. 2: Clustering of water molecules in aqueous solution.

are three and four membered rings, but pure rings of up to 20 molecules were found. These predictions are in good agreement with the reverse MC study of Pálínkás *et al* [2]. What discrepancies there are between their predictions and our simulation results may be the result of a fixed geometry being used in the reverse MC study for representation of the methanol molecule. Visual inspection of some of our methanol clusters has shown that there is appreciable distortion of the local geometry around the methanol hydroxyl, particularly if it is participating in more than one hydrogen bond, as found in the molecules in ring or branched chain structures. In contrast, our results do not support the recent claims of Guo *et al*, that 6- and 8-membered rings are the dominant structural features. We predict that $\sim 30\%$ of clusters contain one or more cyclic motifs (compared to the 50% suggested by Guo *et al* and 33% suggested by Pálínkás *et al*).

Analysis of the lifetimes of the clusters indicate that on average 15% of the clusters are very short-lived, last-

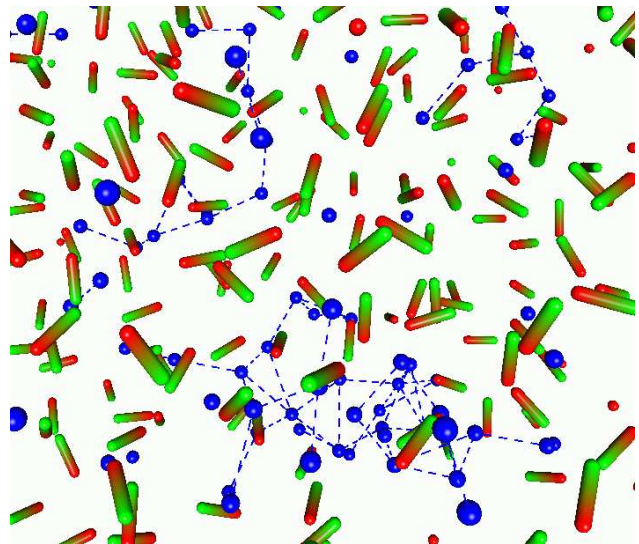


FIG. 3: Visual snapshot of water clustering in 7:3 mixture. Spheres represent water oxygen atoms, sticks represent methanol carbon-oxygen bonds and dashed lines indicate presence of a hydrogen bond between neighbouring water molecules.

ing not more than 1 or 2 ps, whereas others lived for many hundreds of ps. Such an investigation of cluster size and lifetimes precludes the use of *ab initio* simulations to probe such information. The calculations are simply too costly to be able to be performed on a statistically significant number of molecules for a long enough simulation time.

One might expect that a methanol-rich aqueous solution would be homogeneously mixed, as methanol and water are known to be miscible across the entire range of liquid composition. Simulations on the 7:3 methanol-water aqueous solution reveal that the system in fact comprises clusters of water, solvated by the hydrophilic ends of the methanol molecules forming the surrounding fluid. The distribution of water cluster sizes in the mixture is shown in Figure 2 and the overall shape of the distribution appears to be relatively insensitive to system size (results not reported here). What we find is in close agreement with the results of Dixit *et al* on the basis of an EPSR fit to their neutron diffraction data. The results show that water clusters exist within the system, sometimes comprising up to 70% of the water in the simulation box and that only relatively few water molecules ($\sim 12\%$ over the duration of the simulation) are predicted to exist as single molecules, *i.e.* without hydrogen bonds to other neighbouring water molecules. This is the so-called ‘free-swimming’ water that is predicted by Guo *et al* to be incompatible with their results.

A snapshot of a part of the simulation box, illustrating typical configurations is shown in Figure 3; here only water oxygens (spheres) and methanol carbon-oxygen bonds (sticks) are visible for simplicity. The snapshot clearly

shows the presence of a large globular cluster in the lower part of the image, and a more extended, bifurcated chain cluster in the upper part. The large globular cluster has a radius of gyration 5.2 Å and the average hydrogen bond length in the cluster is ~ 2 Å.

We have further analysed the simulation results to calculate an average lifetime of the singleton water molecules. We find that although they account for 12% of all water molecules over the duration of the simulation, they are very short-lived. On average, each single water molecule exists in an unbound state for only a few ps of the simulation. Occasionally, one persists for as long as a few tens of ps, but this is rare. This lifetime is consistent with a picture of dynamic water clusters, frequently shedding and re-absorbing individual water molecules. In contrast, the lifetimes of the larger clusters can be much longer. These can persist in the simulation for hundreds of ps, principally because of the larger cluster sizes. We note that the calculated diffusion coefficients of the water and methanol species in the mixture ($1.5 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ and $1.9 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$, respectively) are both smaller than the corresponding values for the pure components ($2.4 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ and $2.6 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$).

The presence of the water clusters disrupts the hydrogen bond network of methanol molecules. In the mixtures, we find almost double the fraction of methanol clusters existing as 1, 2, or 3 member clusters. If we define a ‘maximum’ cluster size as one that accounts for at least 1% of all clusters of a given species, we find that this threshold is reached at a methanol cluster size of 10 in the mixture simulations, compared with a value of 17 in the pure liquid simulations. The distribution of ring sizes in the methanol clusters in the aqueous solution is similarly affected; 80% of all structures comprise three membered rings and there are no rings larger than hexamers. There is a marked decrease in the percentage of methanol clusters that include a ring structure; this was found to be $\sim 40\%$ in the pure liquid simulation, but drops to $\sim 10\%$ in the mixture. The average lifetime of such clusters is also much shorter compared to those in the pure liquid; in the mixture, the majority of methanol clusters persist for 1ps or less and no cluster survives longer than 40ps.

The intercalation of water into the methanol network is not the only reason for this dramatic change in the hydrogen bonded structures; a compounding reason is that the methyl headgroups of neighbouring methanol molecules are pushed closer together. The evidence for this methanol-methanol association may be probed via the site-site radial distribution functions ($g_{\alpha\beta}$) for methanol in the 7:3 mixture, in comparison with the same functions in the pure liquid. The g_{CC} , g_{HH} (methyl hydrogen) and g_{OO} functions are shown in Figure 4. The RDFs for methanol in the mixture exhibit similar features to those described by Dixit *et al*, namely the first peak in the C-C and the H-H RDFs shift inward slightly. The latter is not found to move as much as seen from the

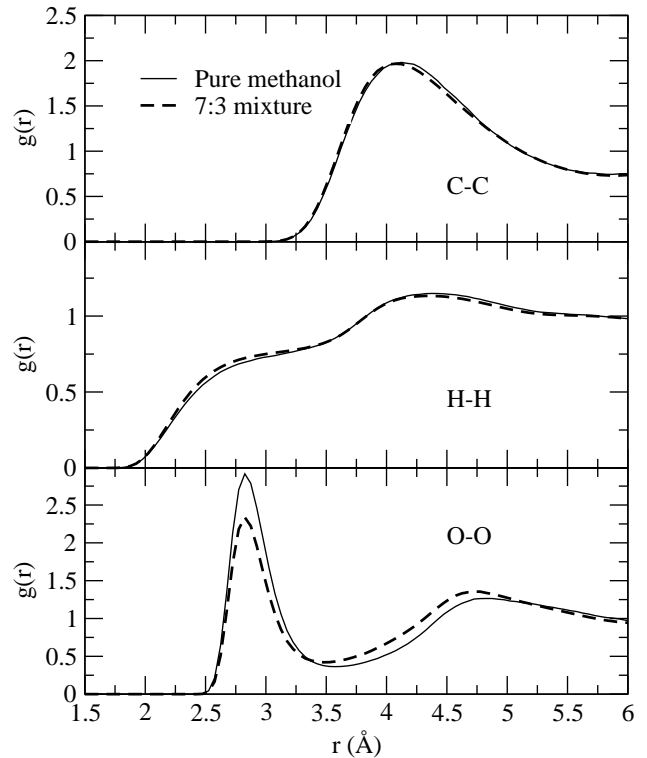


FIG. 4: Site-site radial distribution functions for carbon, methyl hydrogen and oxygen atoms of methanol in the aqueous solution and the pure liquid.

EPSR fitting to experimental results, and this is possibly due to differences in the way internal degrees of freedom are treated in the MD simulations and the EPSR procedure. The first peak of the O-O function diminishes in size and the second peak moves to lower r . These RDFs are consistent with the picture that the methyl groups are compressed in the 7:3 mixture and the hydroxyl groups pushed slightly further apart. Analysis of the corresponding RDFs for the water species in the mixture reveal that the water structure bears many of the signatures of pure water; the peaks in the site-site radial distribution functions are similar to those from the simulations of the pure liquid.

In conclusion, we have applied classical MD simulations to study the structure and dynamical properties of hydrogen-bonded clusters in pure methanol and a 7:3 mole fraction aqueous solution. Contrary to recent claims, we find no evidence of large cyclic structures forming the predominant structural motif in liquid methanol. We predict that the aqueous solution exhibits immiscibility on a microscopic scale, with methanol molecules associating via closer methyl group contact. Work is currently in progress to investigate the temperature and pressure dependence of these phenomena.

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